

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Eva Sevick-Muraca, et al.
Serial No.: 09/870,144
Filing Date: May 30, 2001
Confirmation No. 9131
Art Unit No. 3737
Examiner: W. C. Jung
Title: *Imaging of Light Scattering Tissues with Fluorescent Contrast Agents*

Mail Stop - AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

The following Pre-Appeal Brief Request for Review ("Request") is being filed in accordance with the provisions set forth in the Official Gazette Notice of July 12, 2005 ("OG Notice"). Pursuant to the OG Notice, this Request is being filed concurrently with a Notice of Appeal. The Applicants respectfully request reconsideration of the Application in light of the remarks set forth below.

REMARKS

Applicants contend that the rejection of Claims 1-28 on prior art grounds contain clear legal and factual deficiencies, as described below. In a Final Office Action dated October 19, 2005, Claims 1-34 were rejected as being unpatentable over U.S. Patent No. 6,216,540 to *Nelson ("Nelson")*. Applicants request a finding that these rejections are improper and allowance of these claims.

Procedural History and Introduction

The Final Office Action is the fourth action on the merits for this application. The prior art rejections in each of the first two Office Actions were withdrawn without amendment to the claims, but in response to Applicants noting they were incorrect. Applicants believe the current rejections are similarly improper.

The reasoning provided for the current rejections is somewhat sparse, just as with the previously withdrawn rejections. The Final Office Action's treatment of Applicants' remarks challenging those rejections is even more limited. Applicants respectfully submit that the current rejections are not well-founded for the reasons described in Applicants' Response dated August 4, 2005 at pages 7-9, which are summarized below.¹

The rejection of Claim 1 is improper for at least four reasons:

- the cited reference does not teach or suggest "the agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight;
- the cited reference does not teach or suggest "exposing the tissue to an excitation light" and "detecting a light emission form the tissue in response";
- the cited reference does not teach or suggest that the agent is selected in accordance with a predetermined relationship between degree of image contrast and at least one of fluorescence yield or the fluorescence lifetime; and
- the cited reference does not teach or suggest introducing an exogenous fluorescent contrast agent into a biological tissue.

¹It is noted in the OG Notice at <http://www.uspto.gov/web/offices/com/sol/og/2005/week28/patbref.htm> that "Applicants are encouraged to refer to arguments already of record rather than repeating them in the request." Accordingly, Applicants refer here to, and summarize, the previous arguments rather than reciting them explicitly.

The reasons each of these limitations is not taught or suggested by the cited reference are provided at pages 7-9 of Applicants' Response dated August 4, 2005 and are summarized below. The Final Office Action did not challenge any of these reasons that the four limitations are not disclosed in the cited reference, except for reasons associated with the fourth-listed limitation of "introducing an exogenous fluorescent contrast agent into a biological tissue," but nevertheless continued to reject the claims.

Based on the above-referenced remarks alone, Applicants contend that the rejection of Claim 1 is clearly erroneous and should be withdrawn. However, Applicants provide below additional description of why the above-referenced limitations are not disclosed or suggested by the cited reference.

With respect to the fourth limitation identified above, "introducing an exogenous fluorescent contrast agent into biological tissue," the only one in which the Final Office Action challenged Applicants' assertion that the limitation was missing from the reference, Applicants respectfully submit that the Final Office Action is incorrect. The Final Office Action relies on the radioisotope disclosed at col. 12, lines 34-39 of *Nelson* to teach an exogenous fluorescent contrast agent, but that is incorrect. A radioisotope is not a fluorescent contrast agent, despite the Final Office Action's assertion to the contrary. Further, it is noted that a radioisotope decays spontaneously and cannot be reactivated. As such, excitation light would have no effect on it as it would on fluorophores that would be excited by excitation light. For at least this additional reason, the rejection is improper.

Conceding that the "fluorescence lifetime within a factor of about ten" limitation identified above is not disclosed in the cited reference, the Final Office Action nevertheless concludes that it would have been obvious to vary the fluorescence lifetime "to achieve the claimed invention." Whether or not it would be obvious to vary the fluorescence lifetime, no disclosure exists in the cited references of the desirability of using an agent "having a fluorescence lifetime within a factor of about ten of the mean time-of-flight." For at least this additional reason that this claim limitation is not suggested by the reference, the rejection is improper.

Further, in making this obviousness conclusion, the Final Office Action relies on the flawed premise that the lifetime factor of the fluorescence is a design choice limited by the radiation absorption and how fast the body circulates the materials out of the physiological system. See Final Office Action dated May 21, 2005 at 2-3. Rather, fluorescence lifetime is

not related to the circulation time in the body, but rather is a photophysical property of the contrast agent. Thus, the stated reason that the limitation would have been obvious is clearly incorrect and the rejection is therefore improper, for this additional reason.

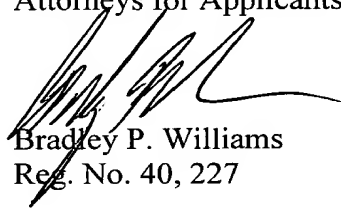
That this limitation would not have been an obvious modification is supported by the fact that the PTO has twice previously withdrawn such an assertion. In particular, the first and second Office Actions alleged that (i) "it would have been an obvious matter of design choice to credit ordinary skill in the art at the time the invention was made to select a contrast agent fitting of said limitation in order to maximize contrast and image clarity," Office Action dated September 12, 2003, page 5, and (ii) "the limitation of the lifetime of the contrast agent is a design choice. However, in both cases, the PTO withdrew the rejection in response to Applicants explaining why the proposal modification was not obvious. *See* Applicants' Response dated January 12, 2004 at 10-13 and January 4, 2005 at 7-9.

The reasons the second and third limitations are not taught or suggested by the cited reference are provided at Page 9 of Applicants' Response dated August 4, 2005. Applicants again note that the Final Office Action did not challenge these remarks. Further, it is noted that no emission wavelength would be generated by using the above radioisotope as a contrast agent, since radioisotopes cannot be excited. For at least these reasons, and the above-referenced reasons described in Applicants' Response dated August 4, 2005 at Pages 7-9, Applicants contend that the rejection of Claim 1 is improper, as is the rejection of Claim 2 through 34 for the same or analogous reasons.

CONCLUSION

As the rejection of Claims 1-34 contains clear deficiencies, Applicants respectfully request a finding of allowance of Claims 1-34. To the extent necessary, the Commissioner is hereby authorized to charge any fees or credit any overpayments to Deposit Account No. 02-0384 of BAKER BOTTS L.L.P.

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Date: January 19, 2006

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